

AD \_\_\_\_\_

Award Number: DAMD17-00-1-0245

TITLE: Robust Detection of Masses in Digitized Mammograms

PRINCIPAL INVESTIGATOR: Lihua Li, Ph.D.

CONTRACTING ORGANIZATION: University of South Florida  
Tampa, Florida 33620

REPORT DATE: June 2001

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20010731 087

**REPORT DOCUMENTATION PAGE**Form Approved  
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

<b>1. AGENCY USE ONLY (Leave blank)</b>		<b>2. REPORT DATE</b> June 2001	<b>3. REPORT TYPE AND DATES COVERED</b> Annual Summary (15 May 00 - 14 May 01)	
<b>4. TITLE AND SUBTITLE</b> Robust Detection of Masses in Digitized Mammograms			<b>5. FUNDING NUMBERS</b> DAMD17-00-1-0245	
<b>6. AUTHOR(S)</b> Lihua Li, Ph.D.				
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> University of South Florida Tampa, Florida 33620  E-Mail: <a href="mailto:lih@moffitt.usf.edu">lih@moffitt.usf.edu</a>			<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>	
<b>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b> U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			<b>10. SPONSORING / MONITORING AGENCY REPORT NUMBER</b>	
<b>11. SUPPLEMENTARY NOTES</b>				
<b>12a. DISTRIBUTION / AVAILABILITY STATEMENT</b> Approved for Public Release; Distribution Unlimited				<b>12b. DISTRIBUTION CODE</b>
<b>13. ABSTRACT (Maximum 200 Words)</b>  This project is to develop a robust computer aided diagnosis (CAD) system for mass detection with high sensitivity and specificity in digitized mammograms. The research scope in past year is on the study of preprocessing and adaptive strategy of CAD modules. Several major progresses have been made including (a) an image standardization algorithm was developed by applying a series of preprocessing to remove extrinsic signal, extract breast area, and normalize the image intensity; (b) multi-mode processing methods were developed by decomposing image features using directional wavelet transform and non-linear multi-scale representation using anisotropic diffusion; (3) adaptive processing in image segmentation using localized adaptive thresholding and adaptive clustering. It is expected that these processing will be very helpful in improving the robustness of the detection system.				
<b>14. SUBJECT TERMS</b> Breast Cancer, Mass, Detection, CAD, Mammography, Robust, Adaptive, Segmentation, Classification				<b>15. NUMBER OF PAGES</b> 21
				<b>16. PRICE CODE</b>
<b>17. SECURITY CLASSIFICATION OF REPORT</b> Unclassified	<b>18. SECURITY CLASSIFICATION OF THIS PAGE</b> Unclassified	<b>19. SECURITY CLASSIFICATION OF ABSTRACT</b> Unclassified	<b>20. LIMITATION OF ABSTRACT</b> Unlimited	

## Table of Contents

Cover.....	1
SF 298.....	2
Table of Contents.....	3
Introduction.....	4
Body.....	4-11
Key Research Accomplishments.....	12
Reportable Outcomes.....	12
Conclusions.....	12
References.....	N/A
Appendices.....	13-21

## INTRODUCTION

This project is to develop a robust computer aided diagnosis (CAD) system for mass detection with high sensitivity and specificity in digitized mammograms. As listed in the Statement of Work, the research scope in the first year of project is on the study of preprocessing and adaptive strategy of CAD modules.

## BODY

***Objective 1: to reduce the variation of mammogram due to non-breast factors before its input to subsequent CAD modules while keep the useful information undistorted.***

### **Accomplishments:**

The images used in CAD algorithm design and testing are obtained mostly by scanning clinical screen film mammograms with digitizers. Due to the difference in film resources and digitizers, and the variation of imaging procedure and characteristics of digitizer, the appearance of digitized images may have a great difference. To reduce the influence of non-breast signals on mass detection, the digitized mammograms are preprocessed. It consisted of three steps:

#### ***A. Breast area extraction***

The mammographic image typically consists of three kinds of regions: (a) unexposed region (part of the image outside the radiation cone); (b) directly exposed image region; and (c) breast region (possibly with pectoral muscles). For an automatic processing being directed to the real breast area, it is necessary to first identify the breast region in a mammogram.

Breast area is extracted by first segmenting the image into foreground and background regions using a histogram derived threshold, then the image is rotated into a position with its chest wall on the left side of the image and the foreground region with largest area being selected as the one that containing breast area; finally the selected region is cropped to get final output. The process of breast area extraction is illustrated in Figure 1, where (c) is the segmented foreground area, its cropping points were marked by arrows, (d) is the final extracted region after cropping.

#### ***B. Removal of extrinsic signals***

The most common extrinsic signals in digitized mammograms include label character, Be-Be mark, scratch distortion, and random pulse noise such as that resulting from dust point on film. The existence of these signals will lead to mis-estimation of characteristics of mammographic image such as maximum value, variance of image, etc, which are usually very important for parameter estimation / selection in CAD algorithm design.

The label characters can be removed in breast area extraction as shown in Fig. 1 because they usually lie outside the breast region. However, most of the Be-Be marks are retained in the image. Furthermore, some large microcalcifications behave like the be-be mark and have a very strong intensity compared to the soft tissues. From the standpoint of mass detection, they can be

taken as an "extrinsic" signal and need to be removed.

A simple plate-filter was specifically designed to detect the Be-Be like signals. The response function of the filter is illustrated in Figure 2. A segmentation of the filtered image is performed based on a global histogram analysis to locate the Be-Be like signals. Because the segmented Be-Be like signal is usually smaller than that of real one, morphological dilation operations are taken to fully cover the Be-Be area. The Be-Be signals are then removed by recursively replacing its pixel intensity value with an average of non-Be-Be pixels of a 3\*3 block. Figure 3 is an example of removal processing of extrinsic signals.

### *C. Image normalization*

Digitized mammographic images can have a very different intensity range in breast area. The possible causes include (1) inherent difference in tissue density for different patients, (2) different film sources may have different exposure extent in X-ray imaging; (3) variation in digitization because of using different digitizers and / or different configurations at different sites for the same type of digitizer. Even though they may not have much negative effect in film screening reading on monitor with manual scaling of the image, it will pose great difficulties in computerized automatic detection of mass because they may result in large deviation in feature distribution. In order to reduce the effect of this kind of variation, as the final step of image standardization, the "cleaned" image is normalized simply by dividing each pixel intensity with the maximum value in each image and rescaled to an intensity range of [255.0 0.0].

***Objective 2: to decompose the complex and difficult detection problem into several relatively simple and easier sub-tasks by means of different image representations.***

### **Accomplishments:**

#### **1. Feature Decomposition Using Directional Wavelet Transform**

Different types of masses tend to be of different image appearance and characteristics. For most of masses, they are primarily related to the region feature. However, for architectural distortion and spiculated masses, their important signs are reflected as directional feature as well as their regional features. Although, for a systematic detection purpose, it will be a great help to utilize both types of features, each may be a "trouble" for another if they are not dealt with appropriately. For example, spiculation is an important feature for detection of stellate mass and classification of malignancy, but it frequently results in the connection of central mass area to surrounding tissue area in mass segmentation. More often is the case when vessels overlap on mass in the projected image, which complicated the segmentation of suspicious regions. Therefore, it is necessary to decompose the mammographic image into a region-based image and line-based image so that each can be processed more efficiently.

Wavelet transform has been proposed as an efficient multiresolution signal representation method. The application of WT in mammogram processing has been explored in feature enhancement, detection of MCC and classification of masses from normal tissue regions. However, for the usual method of building multiresolution analysis and wavelets in 2-D using tensor product, the rectangular decomposition leads to non-isotropic analysis where the horizontal

and vertical direction have a particular importance. To circumvent the drawback of rectangular decomposition in directional selectivity, a directional wavelet transform using radial-angular decomposition was proposed for mammographic feature decomposition as shown in Figure 4. For an input mammographic image, two output feature images were obtained: one is a directional texture image, another is the smoothed version of original image.

## **2. Multi-Scale Representation of Mammogram**

A multi-scale representation of a signal is an ordered set of derived signals intended to represent the original signal at different levels of scale. A major reason for multi-scale representation is to explicitly represent the multi-scale aspect of the data, and to suppress and remove unnecessary and disturbing details such that the later stage processing tasks can be simplified.

Due to fact that the appearance of masses in mammograms has a great variation in size, shape, intensity contrast and intensity variation inside masses, multi-scale description of mammograms can hopefully be effective in revealing the features of different kind of masses at different scale levels, which provides the basis for further multi-mode processing.

There are several approaches to implement multi-scale representation, including the classic methods such as quad-tree, pyramid, and more advanced scale space paradigm such as wavelet analysis. The essential idea is to embed the original image with a set of low-pass filter, such as a set of Gaussian kernels with different variance where larger variances correspond to images of coarser resolutions. However, a major drawback in linear scale-space paradigm is the locations of the region edges can not be well preserved. They are usually shifted from their true locations at the coarser level of multi-scale representation. Because the region boundary and intensity variation of masses are two most important features in mass detection, a meaningful multi-scale description should meet following requirements so that it could be helpful in improving feature extraction and enhancing their discriminability of mass from normal tissue regions:

(a) At each scale level, the object boundary should be well preserved and coincide with the semantically meaningful boundaries at that scale.

(b) The "noise" in regions corresponding to that scale/resolution should be efficiently removed.

(c) it can provide an enhanced morphological definition of the regions at different coinciding scales while suppress the non-coinciding region features.

Anisotropic diffusion (AD) is one of such a "semantically meaningful" description method, and was used for mammogram processing. In this work, two scale images are generated using the AD method, one is of small scale features which is suitable for detection of small to medium size masses; the second is directed to reveal large scale feature and suppress small regions which will be of a help in detection of large-size masses. The Figure 5 shows the 3-D images of region-of-interest (ROI) of a mammogram containing a small and large mass respectively. Their small scale and large scale representations are shown for comparison. It is demonstrated that different masses can be effectively enhanced with different scale representations.

***Objective 3: to make the CAD modules adapt to both temporal (from case to case) and spatial (inside each mammogram) variations.***

## Accomplishments:

### **1. Adaptive Segmentation**

Although different kind of masses may have different radiographic appearance in shape, density, size and/or orientation, most of them have a region with distinctive characteristics from surrounding glandular tissue. For example, the circumscribed masses are typically a circular region with higher density; the malignant spiculated masses generally have a radiographically dense tumor center compared to surrounding tissue. Therefore a region-based detection approach is taken in this method where all the suspicious regions are first separated from fat and glandular normal tissues using image segmentation techniques.

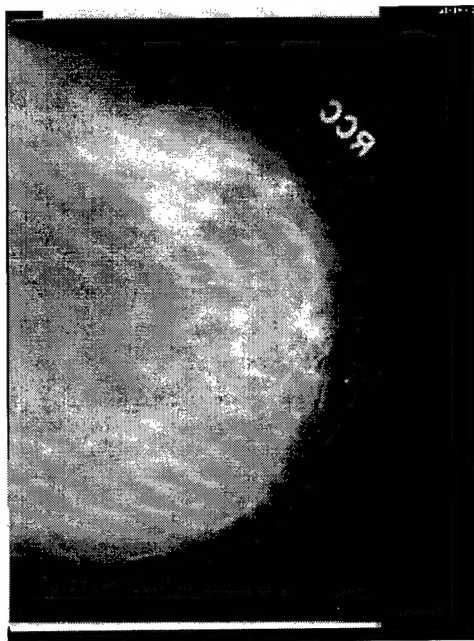
Current image segmentation algorithms can be divided into two broad classes. The first class, region-based methods, attempts to build regions in the images based on the similarity of some characteristics (or features) of the picture elements. The second is boundary-based segmentation methods, which attempts to locate those edges in the image which correspond to object or surface discontinuities, based on differences between pixel characteristics. Because the boundary of mass is frequently difficult to be determined by edge detection due to (a) low contrast for ill-defined mass and the spiculated lesions with blurred borders, (b) the complicated edge feature of the parenchymal tissue, the boundary-based segmentation approach is not suitable for mass segmentation purpose here. On contrast, for different kinds of masses, there is a common distinctive region property from surrounding tissues, such as slowly varying and higher in intensity especially after the preprocessing with filters described above. The region-based segmentation can therefore be appropriately used to segment the suspicious regions. It was performed by two steps:

#### *Step 1: Localized adaptive thresholding*

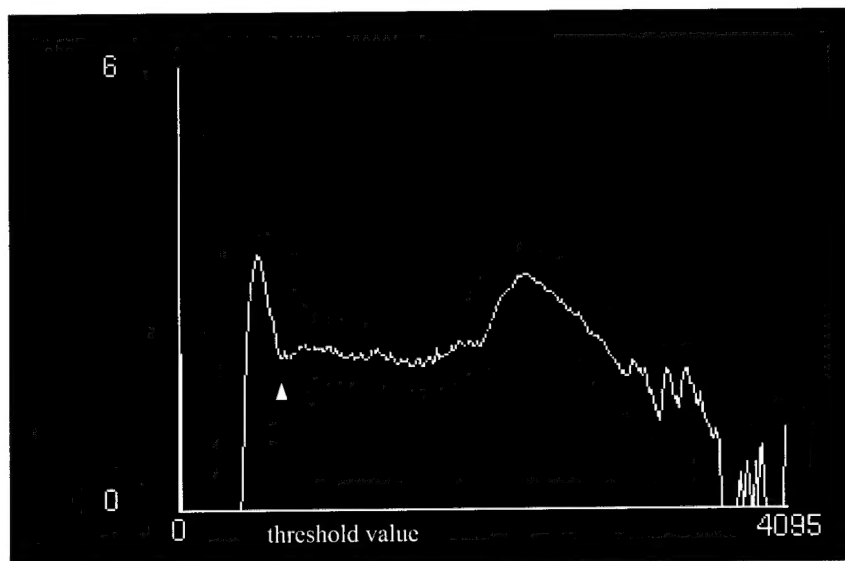
Since mass is generally radiographically denser than surrounding tissue, the locally bright spot of appropriate size is extracted by an initial segmentation using a localized adaptive thresholding method. For each pixel  $I(x,y)$  in breast area, a decision is made to classify it into a potential mass pixel class (class 1) or a normal pixel class (class 2) using an adaptive thresholding method, in which the threshold value has following specific characteristics in segmentation: (a) it is spatially varying, (b) it is double-neighborhood dependent as shown in Figure 6, i.e. a pixel taken to be a potential mass pixel must not only be a dominant point compared to local average but also be a strong spot in a wider neighbor area. To overcome the difficulty of segmentation of masses due to a large variation in size and contrast, two-mode segmentation is performed on the output of multi-scale representation, one is specifically tuned to small-medium size mass (mode S), the other is for medium-large mass segmentation (mode L).

#### *Step 2. Relaxation of segmentation using adaptive clustering*

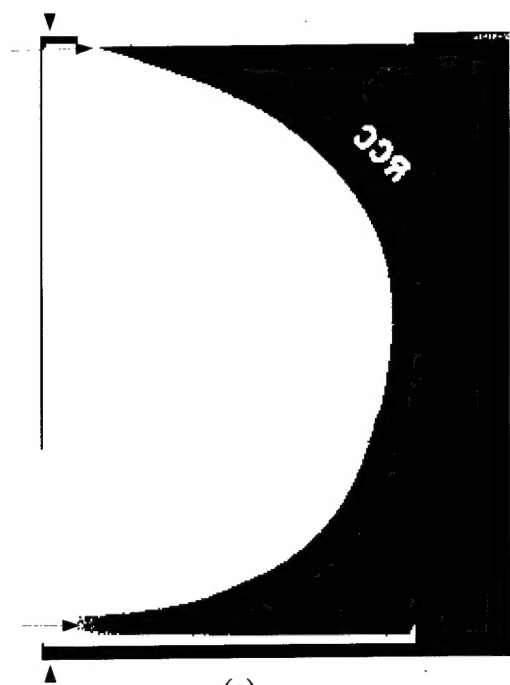
Localized adaptive thresholding provides an efficient approach to separate the potential abnormal pixels especially for low contrast regions. However, because the localized adaptive thresholding is a pixel-based operation, the segmented pixels are usually not well grouped, for example, there are many tiny region with only a couple of pixels; small holes exist in the segmented regions; the boundary of segment is ragged. With localized adaptive thresholding as its initial segmentation, a relaxation process by adaptive clustering is used to refine the segmentation, in which the pixel classification is updated by incorporating local spatial context constraints in the conventional gray-level clustering.



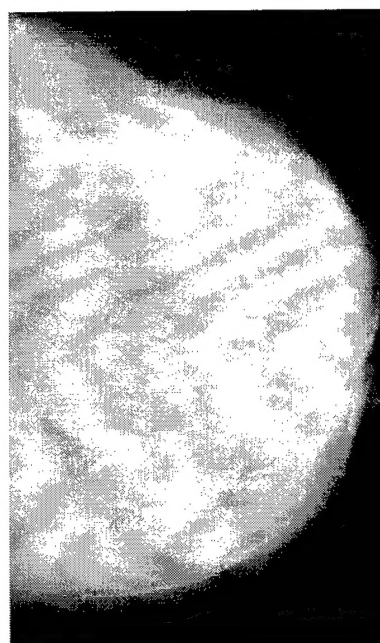
(a)



(b)



(c)



(d)

Fig. 1 Breast area extraction: (a) a typical mammogram with three categories of regions; (b) its histogram of intensity value, the threshold value is derived at the position as indicated by an arrow; (c) segmented image with cropping points indicated; (d) extracted breast image.

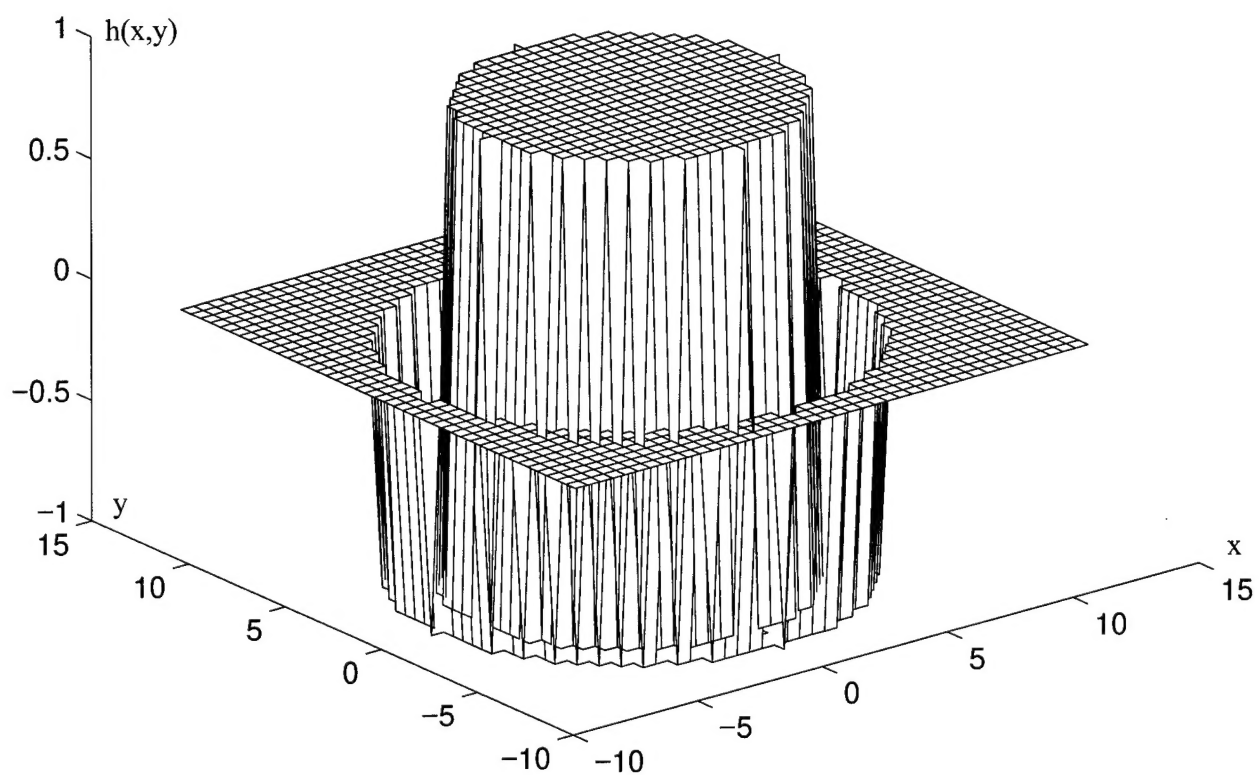


Fig. 2 The response function of plate filter for detecting Be-Be like signals.

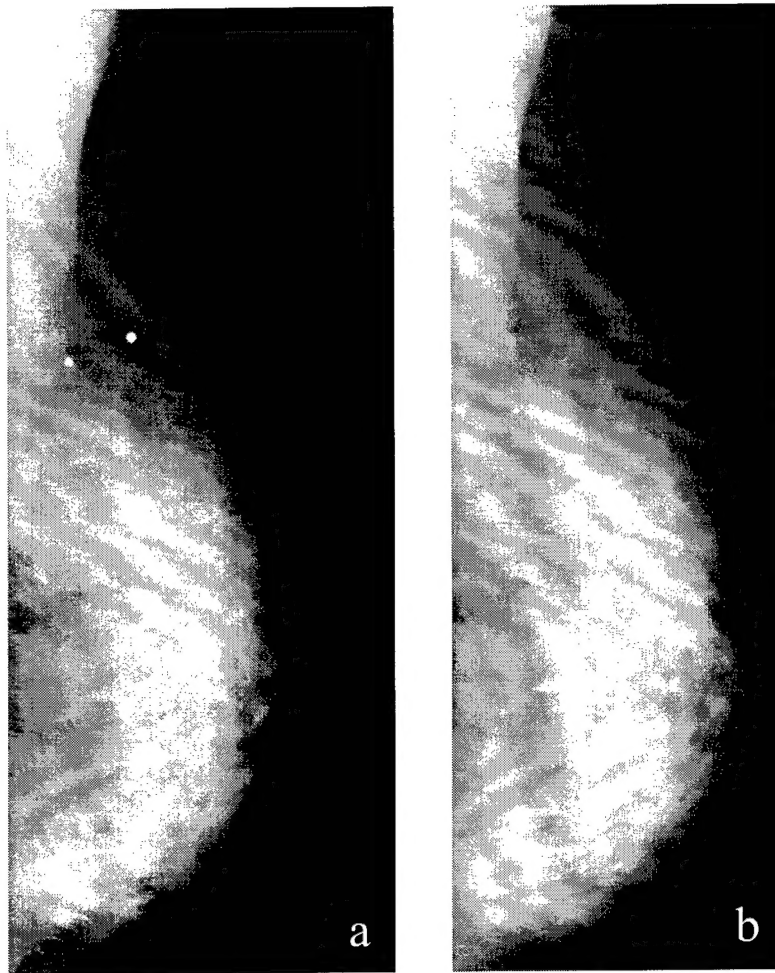


Fig. 3 An example of removal processing of extrinsic signals:  
 (a) A mammogram with a Be-Be mark and a big calcification;  
 (b) the image after removal filtering.

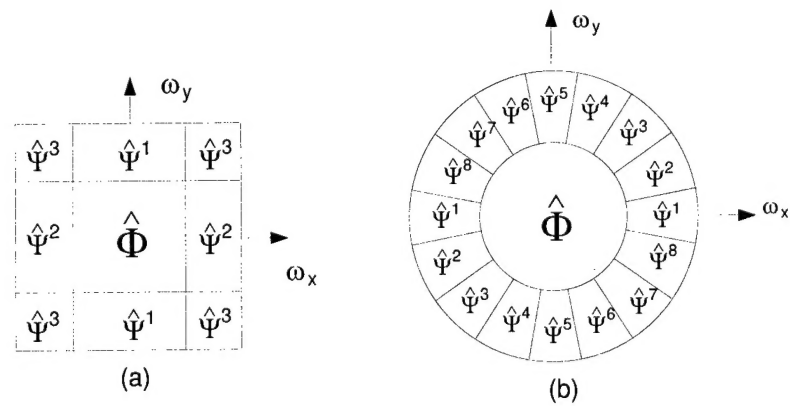


Fig.4 Wavelet transforms with different frequency decomposition:  
 (a) rectangular; (b) radial-angular

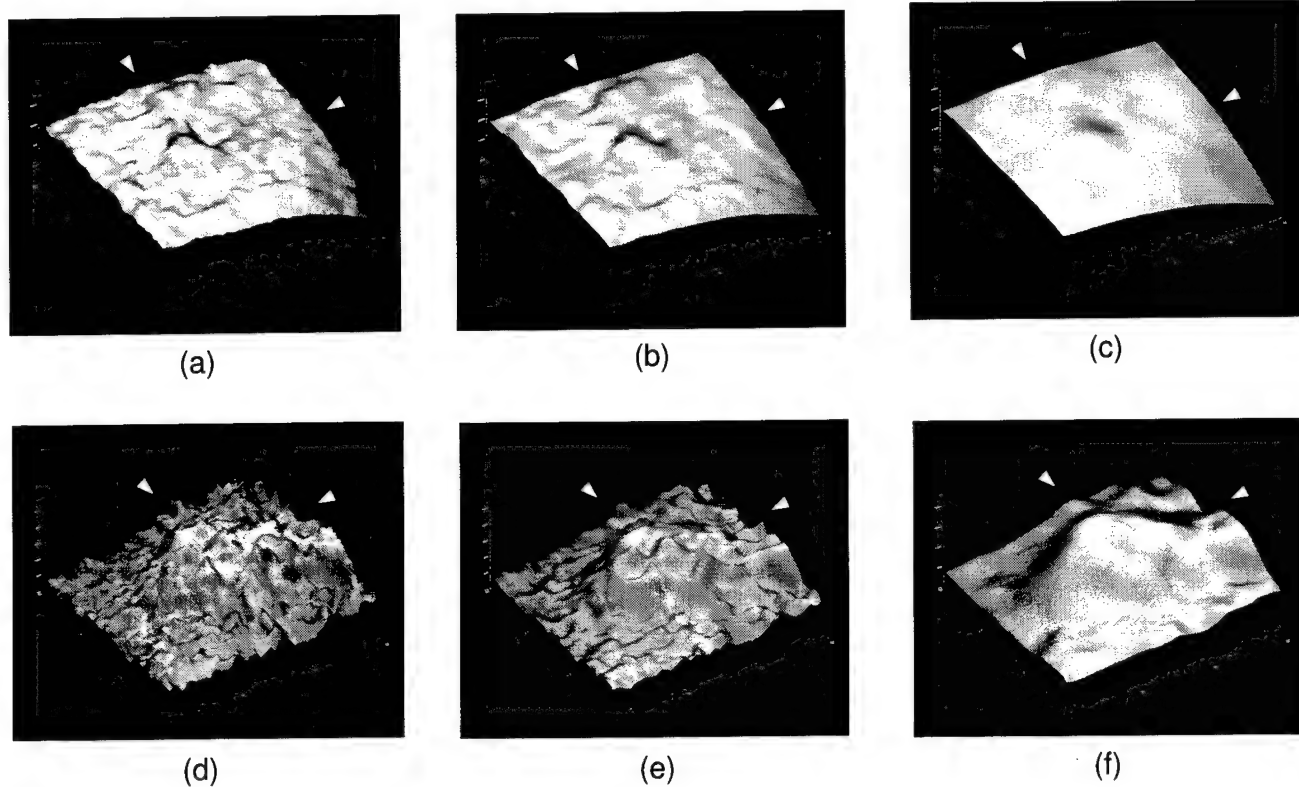


Fig. 5 Nonlinear multi-scale representation of two mammographic ROIs. (a) is a 3-D image of the ROI with a small mass (as the arrows indicated), (b) and (c) are its representations at two different scales; (d) is a 3-D image of the ROI with a large mass (as the arrows indicated), its representations at the same scales as that of (b) and (c) are shown in (e) and (f) respectively.

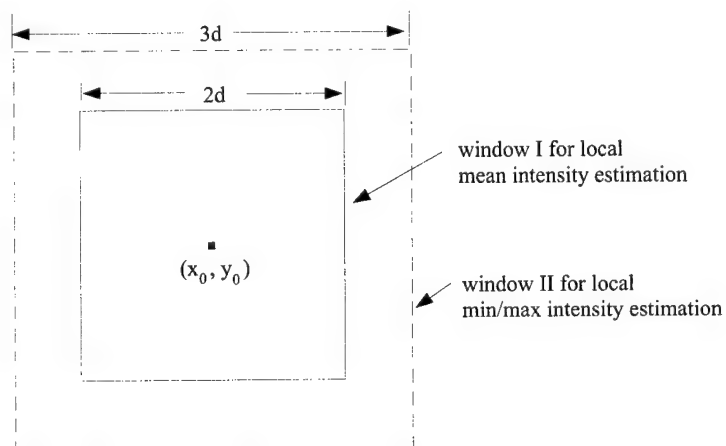


Fig. 6 Windows for localized adaptive thresholding.

## KEY RESEARCH ACCOMPLISHMENTS

1. Image standardization by applying a series of preprocessing to remove extrinsic signal, extract breast area, and normalize the image intensity.
2. Multi-mode processing by decomposing image features using directional wavelet transform (DWT) and non-linear multi-scale representation using anisotropic diffusion (AD).
3. Adaptive processing in image segmentation using localized adaptive thresholding (LAT) and adaptive clustering (AC).

## REPORTABLE OUTCOMES

### *1. Presentation*

Lihua Li, W. Qian, L.P. Clarke, R.A. Clark, J. Thomas, "Improving Mass Detection by Adaptive and Multi-Scale Processing Methods in Digitized Mammograms," Proc. of SPIE Medical Imaging, 1999.

### *2. Fundings Applied*

(a) "Computerized Analysis and Detection of Missed Cancer in Screening Mammogram", a proposal submitted to U.S. ARMY Medical Research and Material Command, BCRP00-IDEA (score 1.8 in Scientific Review).

(b) "An Innovative CAD for Early Detection of Breast Cancer," a proposal submitted to NCI-R21, 2001.

## CONCLUSIONS

The great variation of characteristics of mammograms and masses hinders us in developing a high detection performance and more generalizable CAD system. The typical variations between different mammograms result from either the imaging process (such as film exposure, film label), digitization process (such as spatial / intensity resolution, response function to optical density), and most importantly the inherent breast tissue characteristics. The variations of masses include its size, contrast, shape, location, intensity pattern and its relation to the surrounding tissues. The research work taken in first year of this project proposed several approaches to address these problems. The results have demonstrated their effectiveness.

# Improving mass detection by adaptive and multi-scale processing in digitized mammograms

Lihua Li, Wei Qian, Laurence P. Clarke, Robert A. Clark, Captain Jerry Thomas \*

Department of Radiology, College of Medicine and the H. Lee Moffitt Cancer Center  
and Research Institute at the University of South Florida

\* Uniformed Services University of the Health Sciences, Bethesda, Maryland, Washington DC

## ABSTRACT

A new CAD mass detection system was developed using adaptive and multi-scale processing methods for improving detection sensitivity / specificity, and its robustness to the variations in mammograms. The major techniques developed in system design include (a) image standardization by applying a series of preprocessing to remove extrinsic signal, extract breast area, and normalize the image intensity; (b) multi-mode processing by decomposing image features using directional wavelet transform (DWT) and non-linear multi-scale representation using anisotropic diffusion (AD); (c) adaptive processing in image segmentation using localized adaptive thresholding (LAT) and adaptive clustering (AC); and (d) combined "hard"- "soft" classification by using a modified fuzzy decision tree and committee decision-making method. Evaluations and comparisons were taken with a training dataset containing 30 normal and 47 abnormal mammograms with totally 70 masses, and an independent testing dataset consisting of 100 normal images, 39 images with 48 minimal cancers and 25 images with 25 benign masses. A high detection performance of sensitivity  $TP=93\%$  with false positive rate  $FP=3.1$  per image and a good generalizability with  $TP=80\%$  and  $FP=2.0$  per image are obtained.

**Keywords:** Mass Detection, Adaptive, Multi-Scale Processing, Classification

## 1. INTRODUCTION

Breast cancer is the second leading cause of cancer death among American women. The American Cancer Society projects 181,600 new cases and 44,190 deaths from breast cancer in 1997 [1]. There is considerable evidence that early diagnosis and treatment of breast cancer can significantly increase chances of survival. Of all screening methods currently available, mammography is the most reliable and has demonstrated its benefit in the early detection of breast cancer with mortality reduction of 20-40% [2]. However, because mammogram interpretation is performed by radiologists by visual examination of the films for the presence of abnormalities that may be malignant, the shortage of radiologists and the large volume of mammogram to be analyzed, most of which are normal, make such readings labor intensive, cost ineffective, and often inaccurate. Similarly there is significant inter- and intra-variability in reading mammogram. Studies indicate that, of the breast cancers that are visible in retrospective studies, 10 to 30% are missed during mammographic interpretation, and 40% of the missed cancers appear as masses on the mammogram [3][4]. The missed lesions can be caused by a number of factors, but a significant percentage have been attributed to subjective or varying decision criteria, distraction by other image features, or simple oversight. In an attempt to reduce the cost and increase the effectiveness of mammography, alternative techniques and systems have been developed to improve mammographic imaging and interpretation, among which computer-aided diagnostic (CAD) method is a low cost and efficient approach [5]. There are several examples in the literature of increasing lesion detection through the use of CAD methods [6][7]. However, to date,

there is few practical CAD system for clinical use because (a) they have not achieved sufficient performance (sensitivity and specificity); (b) they have poor reproducibility and adaptivity, i.e. have a great variation in performance for different mammograms at different time and/or sites; (c) their required processing is usually not cost-effective. This paper addresses the first two problems described above in mass detection aiming at improving its detection performance and robustness by making the CAD method adaptive and more generalizable.

## 2. DETECTION METHOD

The new mass detection system is a modification of our previously developed wavelet based detection method by using some novel techniques such as adaptive, nonlinear multiscale processing and hybrid classification methods. Figure 1 shows the schematic diagram of the proposed mass detection system. It is a modular structure and explained as follows.

### 2.1. Preprocessing

The images used in CAD algorithm design and testing are obtained mostly by scanning clinical screen film mammograms with digitizers. Due to the difference in film resources and digitizers, and the variation of imaging procedure and characteristics of digitizer, the appearance of digitized images may have a great difference. To reduce the influence of non-breast signals on mass detection, the digitized mammograms are "standardized" by a series of preprocessing of breast area extraction, removal of Be-Be mark, noise suppression and image intensity normalization.

### 2.2. Feature Decomposition Using Directional Wavelet Transform

Different types of masses tend to be of different image appearance and characteristics. For most of masses, they are primarily related to the region feature. However, for architectural distortion and spiculated masses, their important signs are reflected as directional feature as well as their regional features. Although, for a systematic detection purpose, it will be a great help to utilize both types of features, each may be a "trouble" for another if they are not dealt with appropriately. For example, spiculation is an important feature for detection of stellate mass and classification of malignancy, but it frequently results in the connection of central mass area to surrounding tissue area in mass segmentation. More often is the case when vessels overlap on mass in the projected image, which complicated the segmentation of suspicious regions. Therefore, it is necessary to decompose the mammographic image into a region-based image and line-based image so that each can be processed more efficiently. Directional wavelet transform proposed in our previous work is used here to decompose the mammogram feature [8][9]. For an input mammographic image, two output feature images are obtained: one is a directional texture image, another is the smoothed version of original image.

### 2.3. Multi-Scale Representation of Mammogram

A multi-scale representation of a signal is an ordered set of derived signals intended to represent the original signal at different levels of scale. A major reason for multi-scale representation is to explicitly represent the multi-scale aspect of the data, and to suppress and remove unnecessary and disturbing details such that the later stage processing tasks can be simplified [10]. Due to fact that the appearance of masses in mammograms has a great variation in size, shape, intensity contrast and intensity variation inside masses, multi-scale description of mammograms can hopefully be effective in revealing the features of different kind of masses at different scale levels, which provides the basis for further multi-mode processing. Anisotropic diffusion (AD) is a "semantically meaningful" multi-scale description method [11], and is used for mammogram processing in this work.

The multi-scale representation of image can be considered to be a series of "smoothing" operation, where each "smoothing" operation can be formulated as a diffusive process,

$$\frac{\partial}{\partial t} I(x, y, t) = \Delta (c(x, y, t)) \nabla I(x, y, t) \quad (1)$$

with initial condition  $I(x,y,0)=I_0(x,y)$  be the original image. The diffusion strength is controlled by  $C(x,y,t)$  where  $(x,y)$  is the coordinates of image,  $t$  is the scale-space parameter. Two typical functions are [11]:

$$C_1(x,y,t) = \exp\left(-\left(\frac{|\nabla I(x,y,t)|}{K}\right)^2\right) \quad (2)$$

$$C_2(x,y,t) = \frac{1}{1 + \left(\frac{|\nabla I(x,y,t)|}{K}\right)^{1+\alpha}} \quad \alpha > 0 \quad (3)$$

where parameter  $K$  is chosen according to noise level and edge strength.

To generate different scale representations using AD, we need to determine the diffusion function  $C(*)$ , parameter  $K$  in  $C(*)$ , and the iteration number of diffusion process. Because the flow function with  $C_1$  has a better manageable "band-pass" and edge preservation property,  $C_1(x,y,t)$  is used as the diffusion function in this work. The parameters  $K$  and  $t$  are selected empirically, larger for the representation of mammographic image with large mass and vice versa. In this work, two scale images are generated using the AD method, one is of small scale features which is suitable for detection of small to medium size masses; the second is directed to reveal large scale feature and suppress small regions which will be of a help in detection of large-size masses. Fig. 2 shows the 3-D images of region-of-interest (ROI) of a mammogram containing a small and large mass respectively. Their small scale and large scale representations are shown for comparison in Fig. 2. It is demonstrated that different masses can be effectively enhanced with different scale representations.

#### 2.4. Adaptive Segmentation

A region-based detection approach is taken in this method where all the suspicious regions are first separated from fat and glandular normal tissues using image segmentation techniques.

##### *Step 1: Localized adaptive thresholding*

Since mass is generally radiographically denser than surrounding tissue, the locally bright spot of appropriate size is extracted by an initial segmentation using a localized adaptive thresholding method. For each pixel  $I(x,y)$  in breast area, a decision is made to classify it into a potential mass pixel class (class 1) or a normal pixel class (class 2) by the following rule:

$$I(x,y) \in \text{Suspicious} \quad \text{if } I(x,y) > TH(x,y) \quad (4)$$

$$I(x,y) \in \text{Normal} \quad \text{if } I(x,y) \leq TH(x,y) \quad (5)$$

where  $TH(x,y)$  is an adaptive threshold value calculated by

$$TH(x,y) = M(x,y) + \alpha (I_{\max}(x,y) - I_{\min}(x,y)) \quad (6)$$

where  $M(x,y)$  is an average of the pixel intensity in small window around pixel  $I(x,y)$ ;  $I_{\max}(x,y)$  and  $I_{\min}(x,y)$  are the maximum and minimum intensity value in large window as illustrated in Fig. 3;  $\alpha$  is a thresholding bias coefficient and is chosen empirically.

To overcome the difficulty of segmentation of masses due to a large variation in size and contrast, two-mode segmentation is performed on the output of multi-scale representation, one is specifically tuned to small-medium size mass (mode S), the other is for medium-large mass segmentation (mode L).

##### *Step 2. Relaxation of segmentation using adaptive clustering*

Localized adaptive thresholding provides an efficient approach to separate the potential abnormal pixels especially for low contrast regions. However, because the localized adaptive thresholding is a pixel-based operation, the segmented pixels are usually not well grouped. With localized adaptive thresholding as its initial segmentation, a relaxation process by adaptive clustering is used to refine the segmentation [12], in which the pixel classification is updated by incorporating local spatial context constraints in the conventional gray-level clustering. It is an iterative process:

- (a) with the initial segmentation, calculate an estimate of confidence in the segmentation at each pixel;
- (b) for each pixel, modify the segmentation and the confidence estimate based on the pixels in local region;
- (c) repeat (b) until the segmentation is completed.

The confidence estimate of a pixel  $I(x,y)$  to be a suspicious one (class 1) and normal one (class 2) at  $i$ -th iteration can be described respectively as:

$$\text{class1: } p_1^{(i)} = \exp\{-(I(x,y) - m_1^{(i)}(x,y))^2 + \beta N_1^{(i)}(x,y)\} \quad (7)$$

$$\text{Class2: } p_2^{(i)} = \exp\{-(I(x,y) - m_2^{(i)}(x,y))^2 + \beta N_2^{(i)}(x,y)\} \quad (8)$$

where

$$m_1^{(i)} = \frac{1}{n_1} \sum_{(k,l)} I(k,l) \quad (k,l) \in B_s(x,y) \cap I(k,l) \in \text{Class 1} \quad (9)$$

$$m_2^{(i)} = \frac{1}{n_2} \sum_{(k,l)} I(k,l) \quad (k,l) \in B_s(x,y) \cap I(k,l) \in \text{Class 2} \quad (10)$$

$N_1^{(i)}(x,y)$  and  $N_2^{(i)}(x,y)$  are the number of pixels belonging to Class 1 and Class 2 in the 8-connection neighborhood of  $I(x,y)$  respectively.  $B_s(x,y)$  is a pre-defined neighbor area and decreasing with iteration. The constraint coefficient is  $\beta = 2\sigma^2$ , where  $\sigma^2$  is an estimate of noise variance.

The update of pixel label of  $I(x,y)$  is performed according to following rule:

$$I(x,y) \text{ updated to be Class 1, if } p_1^{(i)} > p_2^{(i)} \quad (11)$$

$$I(x,y) \text{ updated to be Class 2, if } p_1^{(i)} < p_2^{(i)} \quad (12)$$

The relaxation process continues until a criteria is met, such as the number of changed pixels less than a threshold  $T_1$ , and / or the iteration number of relaxation greater than a threshold  $T_2$ .

## 2.5. False-Positive Reduction

A common approach to reduce the FP rate is to perform a further feature analysis of the segmented regions and use a classifier to discriminate masses from normal tissue region. The major difficulties of classification result from the great similarity in appearance between mass and dense normal tissue, and the great variation in feature distribution of different masses. From the classification perspective, the former requires more elaborate features to be extracted for classification while the later means the classifier structure should be more flexible. In this paper, we focus more on the exploration of new classification scheme with less effort on new features design.

Seven features are used in this work for FP reduction including Area, Circularity, Normalized deviation of radial length, Intensity variation, Mean intensity difference, Mean gradient of region boundary, Mean intensity difference along region boundary. They are similar to that we reported before [9] except that (a) one more mixed boundary-intensity feature is added; (b) the calculation of some features is modified with more reasonable

definition.

There are several types of classifiers used in discrimination of masses from normal tissue regions, such as decision tree [13], neural networks [14], linear discriminant analysis (LDA) [15]. A common characteristics of these FP reduction schemes is that a "hard" discriminant criteria is developed by training to evaluate each segmented suspicious region. From the standpoint of region-based classification, it is reasonable, and the task of classifier design is to find an optimal discriminant hyperplane in feature space. However, due to the fact that (1) the mammogram characteristics is usually quite different from case to case; (2) there is a great variation of feature among masses; (3) there is a great similarity between mass and normal tissue regions, the segmented FPs can not be reduced efficiently by a single "hard" decision classifier.

A hybrid classification method is proposed as follows, where the segmented regions are first classified using a modified fuzzy decision tree (MFDT) method. It is a modification of our previously developed fuzzy binary decision tree (FBDT) method [9]. The "hard" decision classifier is then cascaded with a "soft" classification with the objective to reduce FPs in the cases with multiple FPs retained after the "hard" decision classification by an image-based analysis for selecting the best ones among the pre-classified candidate regions as the "real" masses. It is performed by a committee decision method based on a simple premise that most of features of a mass should be top in individual feature ranking among all the candidate suspicious regions in a single mammogram [16].

## 2.6. Combination of Results

There is a great difference of the detected suspicious regions in size and shape from two processing modes. Generally, the small scale processing mode produces more and small detected regions while the large scale processing mode produces fewer and large detected regions. In order to get a single detection output, the detection results from different processing modes have to be combined. In this work, following scheme is proposed for results combination: Taking the detection results from large-scale mode as the major result, using small-scale detection as a reference. For a detected region from small-scale mode, if there is a detection region from large scale mode having a common detection area, we will take the later as the output while discard the former one. On the other hand, for a detection region from small-scale mode, if there is not a detection region from large-scale modes having a common detection area, we will take it as the detected region for output.

## 3. DATABASES AND RESULTS

Two image datasets are generated for mass detection system design and testing. The training dataset contains 30 normal and 47 abnormal mammograms with totally 70 masses. It has the same cases as before for the training of last version of detection algorithm, where the mammograms were digitized by an ImageClear R3000 digitizer (DBA System Inc., Melbourne, FL), so that a comparison of detection performance on training database can be made. The testing dataset was generated independently, consisting of 100 normal images, 39 images with 48 minimal cancers and 25 images with 25 benign masses. It can only be accessed for final testing of algorithm.

The mass detection system is first evaluated with the training database. Fig.4 is a detection FROC curve. The operating point of system is chosen to be at sensitivity  $TP=93\%$  and false positive rate  $FP=3.1$  per image as indicated in Fig. 4. It is then tested independently using the testing database. A good generalization performance was obtained with  $TP=80\%$  and  $FP=2.0$  per image. Two representative mammograms and their detection results are shown in Fig. 5. By analyzing the five masses missed in training at the detection operation point, two of them are due to extremely small size ( $\leq 4$  mm) and lower contrast ( $\leq 4.0$ ); another two of them are on the boundary of breast area where the intensity value decreases dramatically caused by the reduction in thickness at the margin of the compressed breast; one is due to its great deviation of shape feature. Among the testing outputs, a higher detection sensitivity is obtained for benign masses (88%) than that for minimal cancers (75%) at a similar false-positive rate. Again two of the major causes of missing in mass detection are mass located on boundary and lower contrast. In addition to that, a high intensity MCC inside mass is a great interference for mass detection because it results in a great deviation of intensity-related feature values; the masses with too big size could not be detected in testing even though it is not a significant issue from the point of view of CAD.

#### 4. DISCUSSION AND CONCLUSION

The great variation of characteristics of mammograms and masses hinders us in developing a high detection performance and more generalizable CAD system. The typical variations between different mammograms result from either the imaging process (such as film exposure, film label), digitization process (such as spatial / intensity resolution, response function to optical density), and most importantly the inherent breast tissue characteristics. The variations of masses include its size, contrast, shape, location, intensity pattern and its relation to the surrounding tissues. The CAD mass detection method described in this paper proposed a systematic approach to address these problems including (a) image standardization strategy by applying a series of preprocessing to remove extrinsic signal, extract breast area, and normalize the image intensity; (b) multi-mode processing strategy by decomposing image features and multi-scale representation; (c) adaptive processing strategy in localized image segmentation; and (d) combined "hard"- "soft" decision making strategy by using a modified fuzzy decision tree and competitive classification neural network. Compared to the CAD mass detection method we developed earlier, a great improvement is made both in detection performance and generalizability.

#### REFERENCES

- [1] S.L. Parker, T. Tong, S. Bolden and P.A. Wingo. Cancer statistics, 1997. *CA Cancer J Clin*, 47: 5-27, 1997.
- [2] Kerlikowske, D. Grady, S. Rubin, et al., "Efficacy of screen mammography," *JAMA* 1995; 273(2): 149-154.
- [3] R.E. Bird, T.W. Wallace, and B.C. Yankaskas, "Analysis of cancers missed at screening mammography," *Radiology*, vol.184, Sept. 1992.
- [4] M.G. Wallis, M.T. Walsh, and J.R. Lee, "A review of false negative mammography in a symptomatic population," *Clinical Radiology*, vol.44, 1991.
- [5] D.D. Adler, R.L. Wahl, "New methods for imaging the breast: techniques, findings and potential," *AJR*, vol.164, pp.19-30, 1995.
- [6] R.A. Schmidt and R.M. Nishikawa, "Clinical use of digital mammography: The present and the prospects," *Journal of Digital Imaging*, vol.8, no.1, Feb. 1995.
- [7] M. L.Giger, "Computer-aided diagnosis," *RSNA Syllabus: A Categorical Course in Physics, Technical Aspects of Breast Imaging*, eds. AG Haus, MJ Yaffe, 1993; 283-298.
- [8] L. Li, W. Qian, L.P. Clarke, "Wavelet transform for directional feature extraction in medical imaging," *IEEE Proc. of Int. Conf. on Image Processing*, Oct. 1997.
- [9] L. Li, W. Qian, L.P. Clarke, "Digital mammography: computer-assisted diagnosis method for mass detection with multiorientation and multiresolution wavelet transforms," *Academic Radiology* 1997; 4:724-731.
- [10] T. Lindeberg, *Scale-Space Theory in Computer Vision*, Kluwer Academic Publishers, 1994.
- [11] P. Perona, J. Malik, "Scale-space and edge detection using anisotropic diffusion," *IEEE Trans. Pattern Analysis and Machine Intelligence*, Vol.12, July, 1990.
- [12] T. N. Pappas, "An adaptive clustering algorithm for image segmentation," *IEEE Trans. on Signal Processing*, vol.40, no.2, April, 1992.
- [13] W. P. Kegelmeyer, J. M. Pruneda, P. D. Bourland, A. Hillis, M. W. Riggs and M. L. Nipper, "Computer-aided mammographic screen for spiculated lesions," *Radiology*, vol.191, pp.331-337, 1994.
- [14] B. Sahiner, H. P Chan, N. Petrick, D. Wei, M. A. Helvie, D.D. Adler, and M.M. Goodsitt, "Classification of mass and normal breast tissue: A convolution beural network classifier with spatial domain and texture images," *IEEE Trans. Medical Imaging*, Vol. 15, No. 5, Oct. 1995.
- [15] H. P. Chan, D. Wei, M. A. Helvie, B. Sahiner, D. D. Adler, M. M. Goodsitt, N. Petrick, "Computer-aided classification of mammographic masses and normal tissue: linear discriminant analysis in texture feature space," *Phys. Med. Biol.*, vol.40, pp.857-876, 1995.
- [16] D. Black, *The Theory of Committees and Elections*, The Cambridge University Press, 1963.

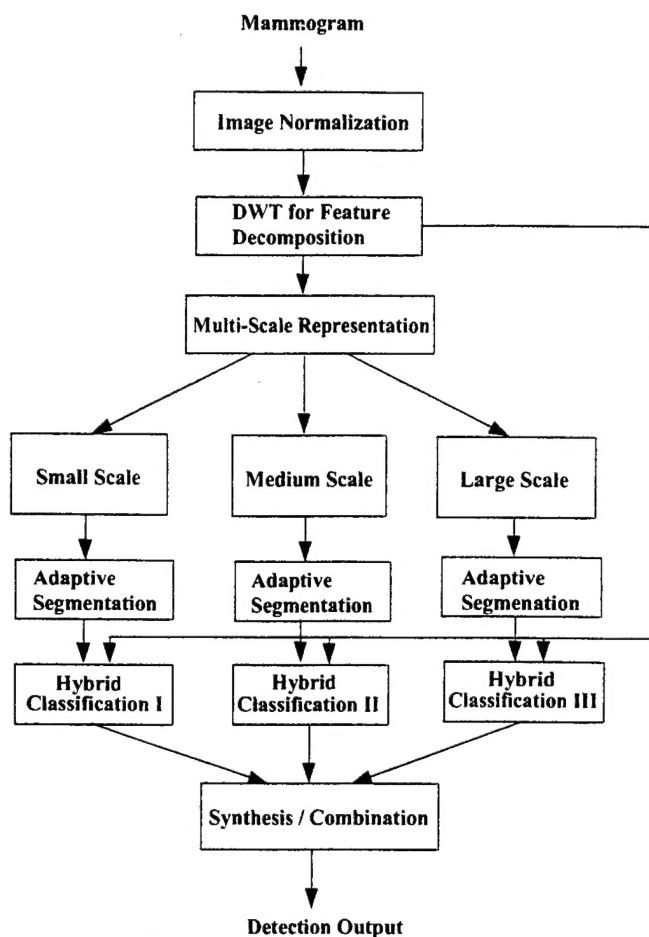


Fig. 1 A schematic diagram of the proposed mass detection system

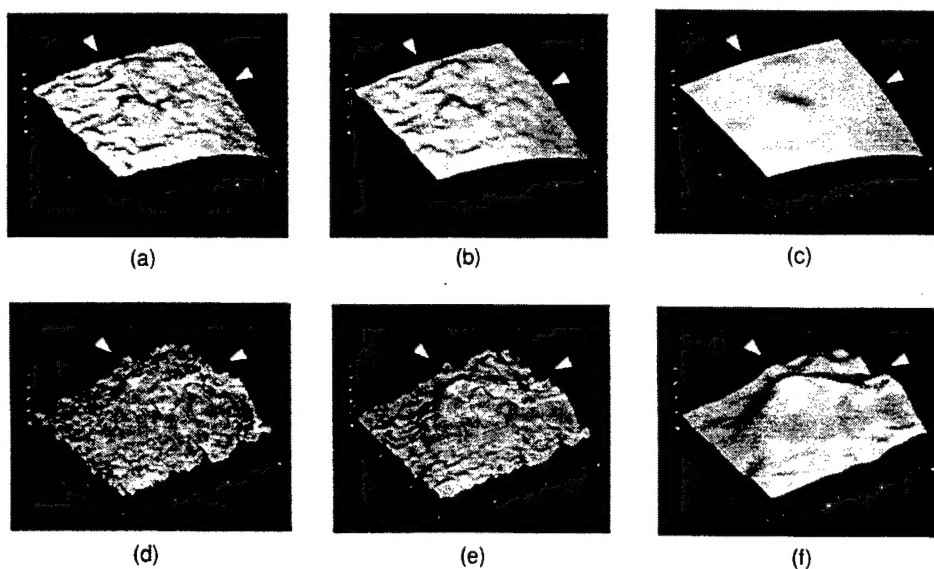


Fig. 2 Nonlinear multi-scale representation of two mammographic ROIs. (a) is a 3-D image of the ROI with a small mass (as the arrows indicated), (b) and (c) are its representations at two different scales; (d) is a 3-D image of the ROI with a large mass (as the arrows indicated), its representations at the same scales as that of (b) and (c) are shown in (e) and (f) respectively.

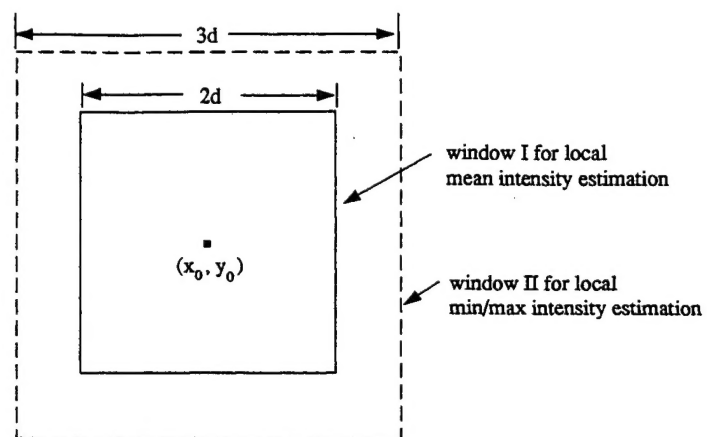


Fig. 3 Windows for localized adaptive thresholding.

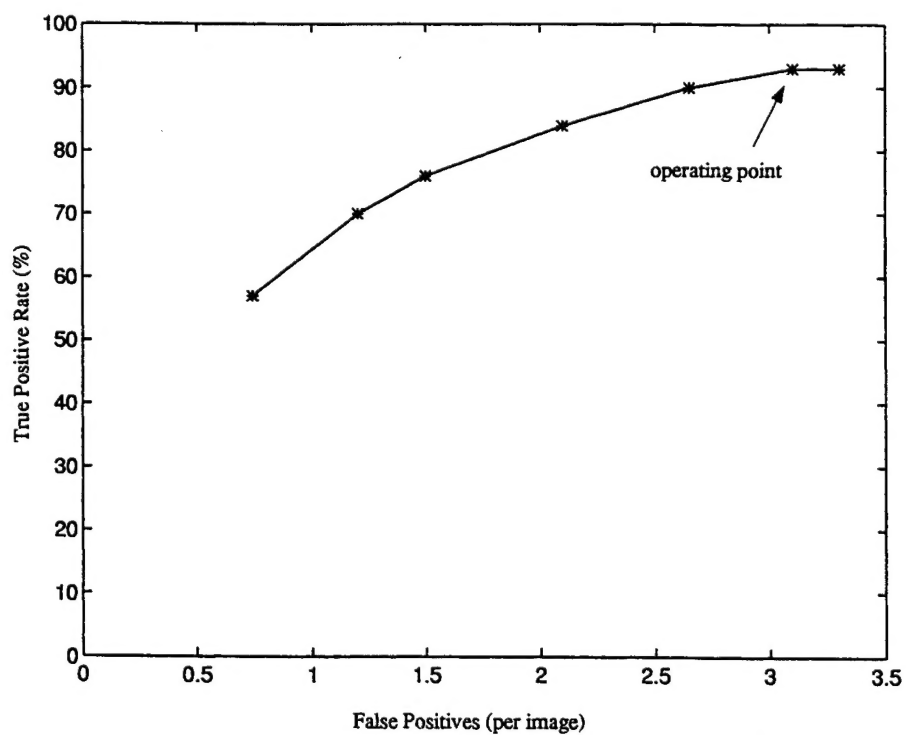


Fig. 4 FROC curves of the true positive detection rate versus the number of false positive findings per image.

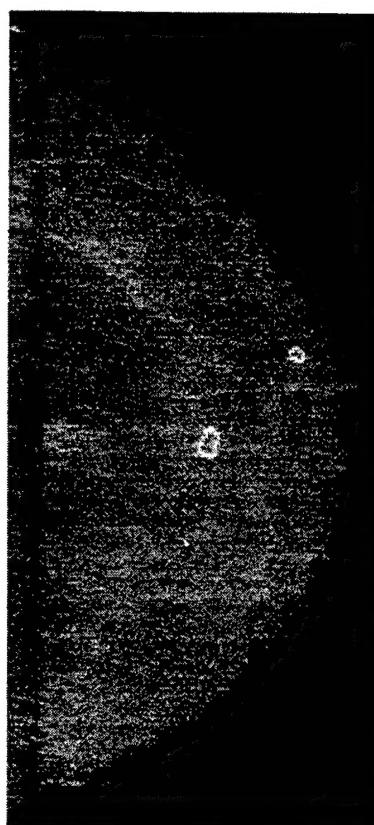
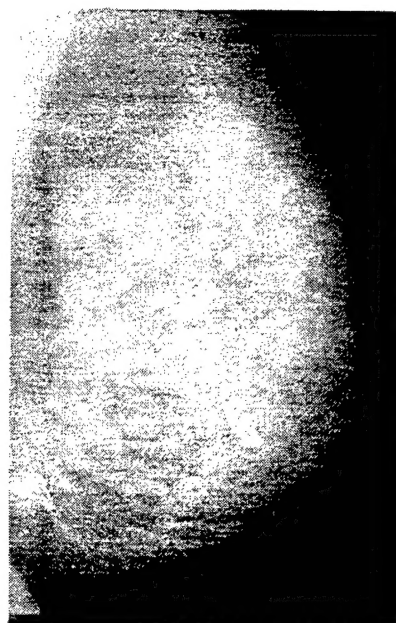
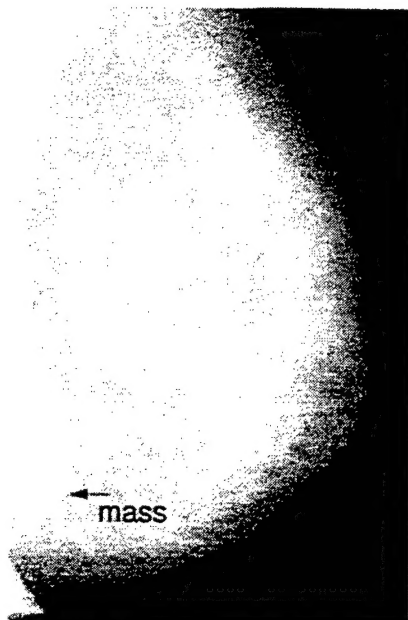


Fig. 5 Two representative mammographic images (preprocessed) and their detection results.